REMARKS

Applicant respectfully requests reconsideration. Claims 1, 2, 4-25, 42 and 86-98 were previously pending in this application. Claims 1, 2, 42 and 87 have been amended. As a result, claims 1, 2, 4-25, 42 and 86-98 are pending for examination with claims 1, 2, 21 and 86 being independent claims. No new matter has been added.

Withdrawn Objections and Rejections

Applicant acknowledges that the Examiner has withdrawn several previous objections and rejections as indicated in the Office Action on pages 2-4.

Rejections under 35 U.S.C. §112

Claim 42 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Without conceding the Examiner's position and rather in the interest of expediting prosecution, Applicant has amended claim 42 to refer to the composition of claim 1, as suggested by the Examiner.

Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 1, 2, 4-20, 87, 90 and 91 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Claims 1 and 2 have been amended to reflect that the amino groups derive from the polysaccharide and not another element in the composition.

Claim 87 has been amended to recite X6 and Y2, as these are defined in claim 86.

In view of these amendments, claims 1, 2 and 87 and claims dependent therefrom are considered definite.

Reconsideration and withdrawal of these rejections is respectfully requested.

Double Patenting Rejection

Claims 1, 2, 4-25, 42 and 86-98 are rejected under the judicially created doctrine of

obviousness-type double patenting over claim 1 of U.S. Patent No. 7,252,828 ("the '828 patent") in view of Fattom et al., *Infect Immun* 66:4588-4592 (1998) ("Fattom"). Claim 18 is rejected under the judicially created doctrine of obviousness-type double patenting over claims 9-11 of the '828 patent in view of Fattom. Applicant respectfully traverses.

An obviousness type double patenting rejection requires that the scope of the asserted and rejected claims be determined, that the difference between these claims be determined, and that these differences be considered obvious to one of ordinary skill in the art.

With respect to the asserted claims, the Examiner states that "the product of claims 1-3 and 9-11 of the ('828 patent) falls within the scope of the ... claims except for the percent of glucosamine amino groups being substituted with acetate". The Examiner further states that the PS/A antigen of claim 1 from the '828 patent has between 50-100% acetate substitutions.

The Examiner has not accurately and fully defined the polysaccharide embraced by claim 1 of the '828 patent. As defined by the specification of the '828 patent, the polysaccharide of claim 1 may be composed of glucose, galactose, and/or glucosamine residues. The glucosamine residues may be acetate-substituted, succinate-substituted, and/or unsubstituted. Moreover, as acknowledged by the Examiner, "the '828 patent does not expressly state that less than 50%, 45%, or 40% of glucosamine amino groups (in the claimed PS/A antigen) ... are substituted with acetate".

The polysaccharide of the rejected claims is composed of glucosamine residues only, and these glucosamine residues are either unsubstituted or substituted with acetate, provided that less than 40% of the glucosamine residues in the claimed composition are acetate substituted. The polysaccharide does not include glucose, galactose or succinate-substituted glucosamine residues.

The polysaccharide of the rejected claims therefore differs from the description of the polysaccharide of the asserted claims in a number of ways, including the lack of glucose, galactose and succinate-substituted glucosamine residues, and the level of acetate substitution of glucosamine residues. The Examiner incorrectly concludes that the only difference between the polysaccharide of the asserted and rejected claims is the level of acetate substitution, and then provides evidence in the form of Fattom to show that this difference is simply an obvious variant of the patented polysaccharide. (The teachings of Fattom are discussed in greater detail below.) The Examiner has completely disregarded the other differences between the claims, and therefore has provided no

evidence of why the remaining differences are obvious modifications of the polysaccharide of claim 1 of the '828 patent. The Examiner is required to consider these differences and provide evidence for why such differences are obvious.

With respect to the difference in acetate substitution level, the Examiner relies on Fattom for the position that deacetylation of polysaccharides is conventional. Fattom analyzes removal of O-linked acetates from CP5 polysaccharide and the immunological effects of such modification. (Fattom does not study the immunological effects of deacetylated CP8 polysaccharide.) The relevance of Fattom's teaching to the claimed invention is questionable for at least two reasons. First, the CP5 polysaccharide studied by Fattom is not the polysaccharide claimed by the '828 patent nor the polysaccharide of the rejected claims. Second, the acetate groups of the Fattom polysaccharide are O-linked acetates while those of the instant invention are N-linked acetates. The conditions for removing O-linked and N-linked acetates are different, with the N-linked conditions generally regarded as harsher. One of ordinary skill in the art would not be able to predict the effect of de-N-acetylation on a polysaccharide (and its immunogenicity) based on the effect of de-O-acetylation of the same polysaccharide (given the different conditions required for the two processes), let alone based on the effect of de-O-acetylation of a different polysaccharide as is the case here.

Moreover, Fattom teaches that antibodies produced against acetylated and de-O-acetylated CP5 conjugates were both opsonic against *S. aureus* strains. Thus, Fattom provides no rationale or motivation for deacetylating, let alone de-N-acetylating, polysaccharides since the acetylated version of the CP5 polysaccharide was sufficiently effective at raising opsonic antibodies as compared to its deacetylated counterpart.

Fattom clearly shows that the role of acetate substitution is unpredictable and varies between different polysaccharides. For example, Fattom states that acetyl-positive *N. meningitidis* group C CP was less immunogenic than its acetyl-negative counterpart but that acetyl-negative *E. coli* K1 capsules were less immunogenic than their acetyl-positive counterparts. Fattom also describes studies reporting that only antibodies specific to acetyl groups on *Salmonella parathyphi* A lipopolysaccharide were bactericidal in an in vitro assay. Finally, Fattom teaches that the O-acetyl moiety of CP5 was the "dominant immunodeterminant among those tested". When taken together,

the data of Fattom and the earlier studies discussed by Fattom do not suggest to one of ordinary skill in the art that all polysaccharides, including that of claim 1 of the '828 patent, should be de-N-acetylated to be immunogenic. In contrast, Fattom explicitly states that in some instances deacetylation is undesirable. What effect de-N-acetylation will have on the immunogenicity of any particular polysaccharide is not predictable based on the teachings of Fattom.

Furthermore, the Examiner provides no basis for why one of ordinary skill in the art would arrive at an acetylated, but not succinylated, glucosamine polysaccharide that does not comprise glucose or galactose residues, as recited in the rejected claims, starting from the polysaccharide of the '828 patent. The teaching in Fattom is insufficient to motivate one of ordinary skill in the art to de-N-acetylate the latter polysaccharide with a reasonable expectation of success. Fattom is also silent regarding glucose, galactose, and succinate-substituted glucosamine residues in polysaccharides, and the Examiner has put forth no other evidence relating to these differences. Accordingly, the instantly claimed polysaccharide is not an obvious variant of the polysaccharide of claim 1 of the '828 patent.

Notwithstanding the foregoing, the claimed polysaccharide possesses properties that are unexpected and could not be predicted based on claim 1 of the '828 patent. As stated repeatedly in the instant specification, the polysaccharide of the rejected claims is able to induce higher titre opsonic antibodies in vivo (compare Fig. 3 (native PNAG) with Fig. 4 (dPNAG) for the total amount of antibody produced, and compare Figs. 5 and 6 (dPNAG) with Figs. 7 and 8 (native PNAG) for the amount of opsonic antibodies in the serum of vaccinated animals). Fig. 9 further shows that much higher levels of opsonic antibodies are produced by vaccination with dPNAG as compared to native PNAG. These differences in opsonic antibody production were unexpected and could not have been predicted a priori. These differences further support the non-obviousness of the polysaccharide of the rejected claims over the polysaccharide of claim 1 of the '828 patent.

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §102

Claims 1, 2, 4-16, 18-24, 42 and 86-97 are rejected under 35 U.S.C. §102(b) as being anticipated by McKenney et al., *Infect Immun* 66:4711-4720 (1998) ("McKenney"). Applicant respectfully traverses.

McKenney does not anticipate the rejected claims because McKenney does not teach each and every limitation of these claims. Specifically, McKenney does not teach a β-1,6 linked glucosamine polymer composed of unsubstituted and acetate-substituted glucosamine residues and, more importantly, lacking succinate-substituted glucosamine residues. McKenney describes a polymer that is 65-100% succinate-substituted. McKenney further states that, in some preparations, the same polymer is also acetylated at levels that are less than 50% of the level of succinate substitution. One of ordinary skill in the art would understand that such a polymer would therefore have both acetate and succinate substitutions. Such a polymer is not embraced by the rejected claims which require that the glucosamine residues be unsubstituted (where R is $-NH_2$) or acetate-substituted (where R is $-NH-CO-CH_3$), but not succinate-substituted.

Later publications have revealed McKenney's polymer characterization to be incorrect, however this mischaracterization is without effect with respect to this (and other) rejections of the claimed invention. The later publications state that McKenney mistakenly observed succinate substitutions but that the polymer was actually highly acetylated instead. Neither the original teaching in McKenney nor the later publications claiming to disclose the correct structure of the polysaccharide anticipate the rejected claims. McKenney does not anticipate the claims, as stated above, because McKenney does not teach a polysaccharide devoid of succinate substitutions. The later publications do not anticipate the claims because they do not teach a glucosamine polymer having less than 40% acetate substitutions. Thus, the claims are not anticipated.

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. §103

Claims 17, 25 and 98 are rejected under 35 U.S.C. §103(a) as being unpatentable over McKenney and further in view of U.S. Patent Publication No. 2002/0119166 to Pier et al. ("Pier"). Applicant respectfully traverses.

As discussed above, McKenney does not anticipate claims 1 and 21 from which claims 17, 25 and 98 depend because McKenney does not teach the isolated polysaccharide of these claims which is explicitly defined as composed of unsubstituted (where R is $-NH_2$) and/or acetate substituted (where R is $-NH-CO-CH_3$) glucosamine residues. The polysaccharide of McKenney contained succinate-substituted glucosamine residues and these are excluded by the definition of the isolated polysaccharide of claims 1 and 21. Pier does not cure the deficiencies of McKenney.

Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 1, 2, 4-25, 42 and 86-98 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 7,252,828 to Pier et al. ("the '828 patent") in view of Fattom. Applicant respectfully traverses.

The rejection is made by applying the '828 patent as prior art under 35 U.S.C. § 102(e). However, the '828 patent and the instant application were commonly owned and subject to an obligation of assignment to a common party at the time the instant claimed invention was made, as evidenced by assignments in both cases from the inventors to Brigham and Women's Hospital, Inc. recorded at Reel/Frame Nos. 012824/0381, 019112/0979 and 014647/0912. Thus, the '828 patent is disqualified as prior art against the claimed invention, and therefore the patent cannot be used as the basis for the stated obviousness rejection.

Reconsideration and withdrawal of this rejection is respectfully requested.

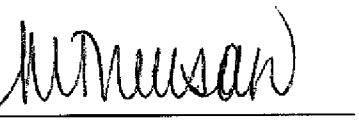
CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. B0801.70255US01.

Dated: September 17, 2008

Respectfully submitted,

By 

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